provided that when X6 is N, then $R^5$ and $R^6$ are not hydrogen.

**[0006]** One embodiment provides a pharmaceutical composition comprising a compound of Formula (I), or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient. One embodiment provides a pharmaceutical composition comprising a compound of Formula (II), or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

**[0007]** One embodiment provides a method of treating cancer in a patient in need thereof, comprising administering to the patient a compound of Formula (I), or a pharmaceutically acceptable salt thereof. One embodiment provides a method of treating cancer in a patient in need thereof, comprising administering to the patient a compound of Formula (II), or a pharmaceutically acceptable salt thereof.

**[0007a]** One embodiment provides the use of a compound of Formula (II) in the manufacture of a medicament for regulating gene transcription in a cell, wherein a bromodomain containing protein is exposed to the compound of Formula (II).

**[0007b]** One embodiment provides the use of a compound of Formula (II) in the manufacture of a medicament for inhibiting of bromodomain-mediated recognition of an acetyl lysine region of a protein, wherein the bromodomain is exposed to a compound of Formula (II).

**[0007c]** One embodiment provides the of a compound of Formula (II), or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating cancer in a patient in need thereof.

**[0007d]** One embodiment provides the use of a compound as described herein in the manufacture of a medicament for regulating gene transcription in a cell, wherein a bromodomain containing protein is exposed to a compound as described herein.

**[0007e]** One embodiment provides the use of a compound as described herein in the manufacture of a medicament for inhibiting of bromodomain-mediated recognition of an acetyl lysine region, wherein the bromodomain is exposed to a compound as described herein.

**[0007f]** One embodiment provides the use of a compound as described herein, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating cancer in a patient in need thereof.

**[0007g]** One embodiment provides the use of a compound of Formula (I) in the manufacture of a medicament for treating cancer and neoplastic disease by regulating gene transcription in a cell, wherein bromodomain containing protein is to be exposed to the compound of Formula (I).

**[0007h]** One embodiment provides the use of a compound of Formula (I) in the manufacture of a medicament for treating cancer and neoplastic disease, wherein the compound of Formula (I) inhibits bromodomain-mediated recognition of an acetyl lysine region of a protein, wherein the bromodomain is to be exposed to a compound of Formula (I).

**[0007i]** One embodiment provides the use of a compound of Formula (I), or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating cancer in a patient in need thereof.

## INCORPORATION BY REFERENCE

**[0008]** All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

## DETAILED DESCRIPTION OF THE INVENTION

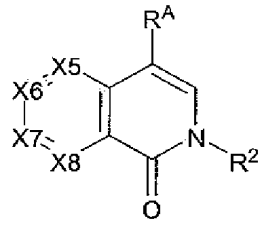
**[0009]** As used herein and in the appended claims, the singular forms "a," "and," and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "an agent" includes a plurality of such agents, and reference to "the cell" includes reference to one or more cells (or to a plurality of cells) and equivalents thereof known to those skilled in the art, and so forth. When ranges are used herein for physical properties, such as molecular weight, or chemical properties, such as chemical formulae, all combinations and subcombinations of ranges and specific embodiments therein are intended to be included. The term "about" when referring to a number or a numerical range means that the number or numerical range referred to is an approximation within experimental variability (or within statistical experimental error), and thus the number or numerical range may vary between 1% and 15% of the stated number or numerical range. The term "comprising" (and related terms such as "comprise" or "comprises" or "having" or "including") is not intended to exclude that in other certain embodiments, for example, an embodiment of any composition of matter, composition, method, or process, or the like, described herein, may "consist of" or "consist essentially of" the described features.

**Definitions**

## CLAIMS

We Claim:

1. A compound of Formula (I), or a pharmaceutically acceptable salt thereof;



Formula (I)

wherein,

$R^2$ is selected from $CH_3$, $CH_2CH_3$, $CH_2CF_3$, $CH_2F$, $CHF_2$, $CF_3$, $CH_2D$, $CHD_2$, or $CD_3$;

X5 is C-$R^5$ or N;

X6 is C-$R^6$ or N;

X7 is C-$R^7$ or N;

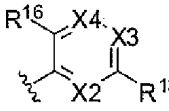
X8 is C-$R^8$ or N; wherein no more than two of X5, X6, X7, or X8 may be N;

$R^5$ is hydrogen, halogen, -OH, -CN, -$OR^{61}$, -$NHR^{61}$, -$N(R^{61})_2$, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, wherein each $R^{61}$ is independently selected from alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

$R^6$ is hydrogen, halogen, -OH, -CN, -$OR^{61}$, -$NHR^{61}$, -$N(R^{61})_2$, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, wherein each $R^{61}$ is independently selected from alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

$R^7$ is hydrogen, halogen, -OH, -CN, -$OR^{61}$, -$NHR^{61}$, -$N(R^{61})_2$, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl, wherein each $R^{61}$ is independently selected from alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

$R^8$ is hydrogen, halogen, or alkyl;

$R^A$ is ;

X2 is N or C-$R^{12}$, wherein $R^{12}$ is hydrogen, halogen, alkyl, or alkoxy;

$R^{13}$ is –Y-Z;

Y is selected from a bond, -$CH_2$-, or –CH($C_1$-$C_4$ alkyl)-;

Z is selected from $-SO_2R^{21}$, $-N(R^{22})SO_2R^{21}$, $-SO_2N(R^{22})_2$, $-N(R^{22})SO_2N(R^{22})_2$, $-CON(R^{22})_2$, $-N(R^{22})CO_2R^{21}$, $-N(R^{22})CON(R^{22})_2$, $-N(R^{22})COR^{21}$, $-COR^{21}$, $-OC(O)N(R^{22})_2$, $-OSO_2N(R^{22})_2$, or $-N(R^{22})SO_3R^{21}$;

X3 is N or C-$R^{14}$, wherein $R^{14}$ is hydrogen, halogen, -CN, alkyl, cycloalkyl, or alkoxy;

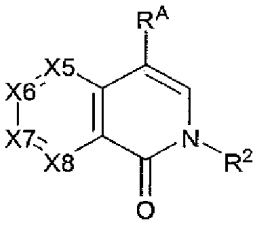
X4 is N or C-$R^{15}$, wherein $R^{15}$ is hydrogen, halogen, alkyl, -CN, or alkoxy;

$R^{16}$ is hydrogen, halogen, -N(H)COX, or –W-X, wherein W is a bond, –O-, -S-, or –NH-, and X is selected from alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, alkynyl, cycloalkylalkynyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

each $R^{21}$ is independently selected from alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl; and

each $R^{22}$ is independently selected from hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl.

2. The compound, or a pharmaceutically acceptable salt thereof, of claim 1, having the structure of Formula (Ib),




Formula (Ib)

wherein,

$R^2$ is selected from $CH_3$;

X5 is C-H;

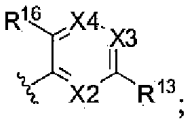
X6 is C-$R^6$;

X7 is C-$R^7$;

X8 is C-H;

$R^6$ is hydrogen, or halogen;

$R^7$ is hydrogen, or halogen;

$R^A$ is 

;

X2 is C-H;

$R^{13}$ is –Y-Z;

Y is selected from a bond, or $-CH_2-$;

Z is selected from $-SO_2R^{21}$, $-N(R^{22})SO_2R^{21}$, $-SO_2N(R^{22})_2$, $-N(R^{22})SO_2N(R^{22})_2$, $-CON(R^{22})_2$, $-N(R^{22})CO_2R^{21}$, $-N(R^{22})CON(R^{22})_2$, $-N(R^{22})COR^{21}$, $-OC(O)N(R^{22})_2$, $-OSO_2N(R^{22})_2$, or $-N(R^{22})SO_3R^{21}$;

X3 is C-$R^{14}$, wherein $R^{14}$ is hydrogen, halogen, $C_1$-$C_3$ alkyl, or $C_1$-$C_3$ alkoxy;

X4 is C-$R^{15}$, wherein $R^{15}$ is hydrogen, or halogen;

$R^{16}$ is –W-X, wherein W is a bond, –O-, -S-, or –NH-, and X is selected from alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

each $R^{21}$ is independently selected from alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl; and

each $R^{22}$ is independently selected from hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl.

3. The compound, or a pharmaceutically acceptable salt thereof, of claim 2, wherein $R^6$ is halogen, and $R^7$ is hydrogen.

4. The compound, or a pharmaceutically acceptable salt thereof, of claim 2, wherein $R^6$ is hydrogen, and $R^7$ is halogen.

5. The compound, or a pharmaceutically acceptable salt thereof, of claim 2, wherein $R^6$ is hydrogen, and $R^7$ is hydrogen.

6. The compound, or a pharmaceutically acceptable salt thereof, of claim 2, wherein Y is $-CH_2-$.

7. The compound, or a pharmaceutically acceptable salt thereof, of claim 6, wherein Z is $-SO_2R^{21}$, or $-N(R^{22})SO_2R^{21}$.

8. The compound, or a pharmaceutically acceptable salt thereof, of claim 2, wherein Y is a bond.

9. The compound, or a pharmaceutically acceptable salt thereof, of claim 8, wherein Z is $-N(R^{22})SO_2R^{21}$, or $-N(R^{22})SO_2N(R^{22})_2$.

10. The compound, or a pharmaceutically acceptable salt thereof, of claim 8, wherein Z is $-SO_2R^{21}$.

11. The compound, or a pharmaceutically acceptable salt thereof, of claim 8, wherein Z is $-SO_2N(R^{22})_2$.

12. The compound, or a pharmaceutically acceptable salt thereof, of claim 10, wherein $R^{21}$ is heterocyclyl, or heterocyclylalkyl.

13. The compound, or a pharmaceutically acceptable salt thereof, of claim 9, wherein $R^{22}$ is hydrogen or methyl.

14. The compound, or a pharmaceutically acceptable salt thereof, of claim 11, wherein at least one $R^{22}$ is alkyl, cycloalkyl, or aralkyl.

15. The compound, or a pharmaceutically acceptable salt thereof, of claim 10, wherein $R^{21}$ is alkyl, cycloalkyl, or cycloalkylalkyl.

16. The compound, or a pharmaceutically acceptable salt thereof, of claim 15, wherein the alkyl is a $C_1$-$C_4$ alkyl.

17. The compound, or a pharmaceutically acceptable salt thereof, of claim 2, wherein $R^{14}$ is hydrogen, and $R^{15}$ is hydrogen.

18. The compound, or a pharmaceutically acceptable salt thereof, of claim 2, wherein W is a bond or –NH-.

19. The compound, or a pharmaceutically acceptable salt thereof, of claim 2, wherein W is –O-.

20. The compound, or a pharmaceutically acceptable salt thereof, of claim 18, wherein X is alkyl.

21. The compound, or a pharmaceutically acceptable salt thereof, of claim 19, wherein X is alkyl.

22. The compound, or a pharmaceutically acceptable salt thereof, of claim 18, wherein X is cycloalkylalkyl.

23. The compound, or a pharmaceutically acceptable salt thereof, of claim 19, wherein X is cycloalkylalkyl.

24. The compound, or a pharmaceutically acceptable salt thereof, of claim 18, wherein X is aryl.

25. The compound, or a pharmaceutically acceptable salt thereof, of claim 19, wherein X is aryl.

26. The compound, or a pharmaceutically acceptable salt thereof, of claim 16, wherein the $C_1$-$C_4$ alkyl is a $C_1$ alkyl.

27. The compound, or a pharmaceutically acceptable salt thereof, of claim 2, wherein Y is a bond, Z is $-SO_2R^{21}$, W is –O-, and X is aryl or cycloalkylalkyl.

28. A compound, or a pharmaceutically acceptable salt thereof, selected from:

N-[4-methyl-3-(2-methyl-1-oxoisoquinolin-4-yl)phenyl]methanesulfonamide;

4-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-6-fluoro-2-methylisoquinolin-1-one;

4-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-7-fluoro-2-methylisoquinolin-1-

one;

4-[2-(2,4-difluorophenoxy)-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

N-[4-(2,4-difluorophenoxy)-3-(2-methyl-1-oxoisoquinolin-4-yl)phenyl]ethanesulfonamide;

4-[2-(cyclopropylmethoxy)-5-ethylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-[2-(cyclopropylmethoxy)-5-ethylsulfonylphenyl]-6-fluoro-2-methylisoquinolin-1-one;

2-methyl-4-[5-methylsulfonyl-2-(oxolan-3-yloxy)phenyl]isoquinolin-1-one;

2-methyl-4-[5-methylsulfonyl-2-(oxan-4-yloxy)phenyl]isoquinolin-1-one;

4-(2-ethoxy-5-methylsulfonylphenyl)-2-methylisoquinolin-1-one;

2-methyl-4-(5-methylsulfonyl-2-propoxyphenyl)isoquinolin-1-one;

2-methyl-4-[5-methylsulfonyl-2-(oxan-3-yloxy)phenyl]isoquinolin-1-one;

4-[2-(trans-4-hydroxycyclohexyl)oxy-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-[5-ethylsulfonyl-2-(trans-4-hydroxycyclohexyl)oxyphenyl]-2-methylisoquinolin-1-one;

4-[2-(trans-4-aminocyclohexyl)oxy-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-[2-(cis-4-aminocyclohexyl)oxy-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-(2-but-2-ynoxy-5-methylsulfonylphenyl)-2-methylisoquinolin-1-one;

4-(2-but-2-ynoxy-5-ethylsulfonylphenyl)-2-methylisoquinolin-1-one;

6-fluoro-4-[2-(trans-4-hydroxycyclohexyl)oxy-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

7-fluoro-4-[2-(trans-4-hydroxycyclohexyl)oxy-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-[5-ethylsulfonyl-2-(trans-4-hydroxycyclohexyl)oxyphenyl]-6-fluoro-2-methylisoquinolin-1-one;

4-[5-ethylsulfonyl-2-(trans-4-hydroxycyclohexyl)oxyphenyl]-7-fluoro-2-methylisoquinolin-1-one;

2-methyl-4-[5-methylsulfonyl-2-(oxolan-3-ylamino)phenyl]isoquinolin-1-one;

2-methyl-4-[5-methylsulfonyl-2-(oxan-4-ylamino)phenyl]isoquinolin-1-one;

4-[2-[(trans-4-hydroxycyclohexyl)amino]-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-[2-(cyclopropylmethylamino)-5-ethylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-[2-(cyclopropylmethylamino)-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-[2-(cyclopropylmethylamino)-5-ethylsulfonylphenyl]-7-fluoro-2-methylisoquinolin-1-one;

4-[2-(cyclopropylmethylamino)-5-methylsulfonylphenyl]-7-fluoro-2-methylisoquinolin-1-one;

4-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-2-methyl-6-(trifluoromethyl)isoquinolin-1-one;

4-[2-(cyclopropylmethoxy)-5-methylsulfonylphenyl]-6-methoxy-2-methylisoquinolin-1-one;

[4-(cyclopropylmethoxy)-3-(2-methyl-1-oxoisoquinolin-4-yl)phenyl] sulfamate;

N-[2-(2-methyl-1-oxoisoquinolin-4-yl)-4-methylsulfonylphenyl]-cyclopropanecarboxamide;

N-[2-(2-methyl-1-oxoisoquinolin-4-yl)-4-methylsulfonylphenyl]propanamide;

N-[2-(2-methyl-1-oxoisoquinolin-4-yl)-4-methylsulfonylphenyl]acetamide;

2-methyl-4-(5-methylsulfonyl-2-propylphenyl)isoquinolin-1-one;

4-(2-ethyl-5-methylsulfonylphenyl)-2-methylisoquinolin-1-one;

4-(2-butyl-5-methylsulfonylphenyl)-2-methylisoquinolin-1-one;

4-[2-(2-cyclopropylethyl)-5-methylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-[2-(cyclopropylmethoxy)-5-propan-2-ylsulfonylphenyl]-2-methylisoquinolin-1-one;

4-[2-(cyclopropylmethoxy)-5-propan-2-ylsulfonylphenyl]-6-methoxy-2-methylisoquinolin-1-one;

4-[5-(ethylsulfonylmethyl)-2-(2,2,2-trifluoroethoxy)phenyl]-2-methylisoquinolin-1-one; and

2-methyl-4-[5-(methylsulfonylmethyl)-2-(2,2,2-trifluoroethoxy)phenyl]isoquinolin-1-one.

29. A pharmaceutical composition comprising a compound of Formula (I) as described in claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

30. A pharmaceutical composition comprising a compound of claim 28, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

31. Use of a compound of Formula (I) in the manufacture of a medicament for treating cancer and neoplastic disease by regulating gene transcription in a cell, wherein bromodomain containing protein is to be exposed to the compound of Formula (I).
32. Use of a compound of Formula (I) in the manufacture of a medicament for treating cancer and neoplastic disease, wherein the compound of Formula (I) inhibits bromodomain-mediated recognition of an acetyl lysine region of a protein, wherein the bromodomain is to be exposed to a compound of Formula (I).
33. Use of a compound of Formula (I), or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating cancer in a patient in need thereof.